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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,628	04/04/2007	Christian Peter Petzelt	31304-764.831	8178

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EXAMINER	
ARNOLD, ERNST V	
ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,628	PETZELT ET AL.	
	Examiner	Art Unit	
	ERNST V. ARNOLD	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-11 have been cancelled. Claims 12-24 are under examination.

Comment: Please insert the continuity data at the top of page 1.

Information Disclosure Statement

Foreign language references have only been considered to the extent that an English language abstract, translation or equivalent has been provided.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for preventing or reducing cellular damage of tissue or organs to be transplanted in a human; preventing or reducing apoptotic cell death after eye laser surgery; protecting endothelial cells of the intestine in sepsis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention without an undue amount of experimentation. This is a full enablement rejection.

Let the Examiner be clear: Applicant is not enabled for preventing or reducing cellular damage of tissue or organs to be transplanted in a human; preventing or reducing apoptotic cell death after eye laser surgery; protecting endothelial cells of the intestine in sepsis.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation. While all of the factors have been considered, only those required for a prima facie case are set forth below.

2) Nature of the invention

The nature of the invention is directed to methods for treating a human comprising administering an effective amount of xenon for **preventing or reducing cellular damage of tissue or organs to be transplanted in a human; preventing or reducing apoptotic cell death after eye laser surgery; protecting endothelial cells of the intestine in sepsis.**

3) Relative level of skill possessed by one of ordinary skill in the art

From MPEP 2141.03: **The "hypothetical person having ordinary skill in the art' to which the claimed subject matter pertains would, of necessity have the capability of understanding the scientific and engineering principles applicable to the pertinent art**." *Ex parte Hiyamizu*, 10 USPQ2d 1393, 1394 (Bd. Pat. App. & Inter. 1988) (The Board disagreed with the examiner's definition of one of ordinary skill in the art (a doctorate level engineer or scientist working at least 40 hours per week in semiconductor research or development), **finding that the hypothetical person is not definable by way of credentials**, and that the evidence in the application did not support the conclusion that such a person would require a doctorate or equivalent knowledge in science or engineering.). (Emphasis added).

4) State of, or the amount of knowledge in, the prior art

The art teaches that apoptosis is a complex series of cellular events (Taylor et al. Nature Reviews 2008, 9, 231-241; see figures 1-3 for example). The art teaches that xenon is a neuroprotectant because it is an NMDA antagonist ((page 1485 Abstract and introduction) Wilhelm et al. Anesthesiology 2002, 96, 1485-91).

5) Level or degree of predictability, or a lack thereof, in the art

Apoptosis is a complex mechanism where much is left unknown. Taylor et al. concede that "significant gaps remain in our knowledge of the process." (page 239 conclusions).

6) Amount of guidance or direction provided by the inventor

Applicant was required to provide in the specification additional guidance and direction with respect to how use the claimed subject matter in order for the application to be enabled with respect to the full scope of the claimed invention. Applicant performed a series of experiments on cortical neurons and HeLa cells by inducing apoptosis with staurosporine and treating with

xenon. However, the art has already shown xenon to be a neuroprotectant and these results appear to be expected results. In addition, there is a lack of guidance in the specification as to how one would extrapolate the cell based neuroprotection experiments to cellular damage, apoptotic cell death after laser eye surgery or protecting against sepsis. Applicant has not provided any examples of **preventing or reducing cellular damage of tissue or organs to be transplanted in a human; preventing or reducing apoptotic cell death after eye laser surgery; protecting endothelial cells of the intestine in sepsis** that would guide or direct one of ordinary skill in the art to performing the instantly claimed methods.

7) Presence or absence of working examples

The specification fails to provide scientific data and working embodiments with respect to **preventing or reducing cellular damage of tissue or organs to be transplanted in a human; preventing or reducing apoptotic cell death after eye laser surgery; protecting endothelial cells of the intestine in sepsis.** In addition, the examples provided do not appear art recognized models for the claimed subject matter. The only experiments disclosed appear to confirm that which is already known in the art; that xenon protects cells (See examples 1 and 2 of WO 00/53192 and the disclosure of Petzelt et al. Life Sciences 2003, 72, 1909-1918).

8) Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure

One of ordinary skill in the art would have to conduct a myriad number of experiments comprising determining dosage amounts of xenon/xenon gas mixtures; administration routes and then testing by trial and error every combination on patients where our current state of knowledge has significant gaps and the outcome could be death. Without any guidance on how

to extrapolate the data provided by Applicant, essentially one of ordinary skill in the art has to figure out how to do this themselves. As a result, one of ordinary skill in the art would be required to conduct an undue amount of experimentation to see if the method for preventing or reducing cellular damage of tissue or organs to be transplanted in a human; preventing or reducing apoptotic cell death after eye laser surgery; protecting endothelial cells of the intestine in sepsis actually works.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable." (Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997)).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12 and 16-24 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/53192 (Hereinafter '192).

192 discloses the use of xenon or xenon gas mixtures for treating neurointoxications such as apoplexy (stroke), Parkinson's and craniocerebral trauma (Claims 1, 4, 7, 8 and 16). The

Examiner interprets this to mean methods of using the composition. It is also the Examiner's position that at least one of the neurointoxications disclosed by '192 is an aberrant or undesired apoptosis or a disease associated with aberrant apoptosis in the absence of evidence to the contrary. The Examiner notes that the instant specification on page 4 describes ischemia reperfusion injury and the production of hydrogen peroxide associated with the injury which is similar to stroke as diseases associated with aberrant apoptosis. In this way, claim 12 is anticipated. '192 discloses a preparation that contains **5 to 90%** by volume xenon (claim 12) and a preparation that contains **5 to 30%** by volume xenon (claim 13). The preparation can further contain **oxygen and/or nitrogen and/or air** (claim 14 and 17). Thus, instant claims 16-19 are anticipated. The preparation has a ratio of xenon to oxygen of **80 to 20%** by volume which reads on instant claims 20 - 23 (claim 15). (Once mixed, the product is obtained.) A method of producing the preparation by mixing xenon with another gas harmless to humans is disclosed (claims 18 and 19). The resulting gas mixture reads on instant claim 21. Mixing with air (another gaseous compound) reads on instant claim 24.

Claim Rejections - 35 USC § 102

Claims 12, 16 and 18-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Franks et al. (US 6274633).

Franks et al. disclose methods of preparing anesthetic solutions in column 7, lines 40-62 which anticipate instant claims 21-23.

Preparation of Anaesthetic Solutions

Xenon solutions were prepared by first bubbling pure gases (oxygen, nitrogen or xenon) through fine sintered-glass bubblers in 250- or 500-ml Drechsel bottles filled with extracellular recording saline. Solutions were bubbled for 1.5–2 hours, although equilibrium was found to occur within 45 minutes. (To minimise oxidization, the neurotoxins and neurotransmitters were excluded from the fully oxygenated saline.) During bubbling, the solutions were continually stirred at room temperature. These solutions were then mixed to achieve the desired final concentrations of the gases. Our control solutions usually contained 80% of the nitrogen solution and 20% of the oxygen solution, while our test solutions usually contained 80% of the xenon solution and 20% of the oxygen solution. Using a Bunsen water/gas partition coefficient of 0.0965 (Smith R A et al, Biochim. Biophys. Acta 1981, 645:327–338) we calculate that our standard test solution contained 3.4 mM xenon. Xenon (research grade, 99.993% pure) was supplied by BOC gases, Guildford, Surrey, UK. In all cases xenon was pre-applied to the neurons for at least 30 seconds before the initiation of synaptic currents.

Franks et al. claim method of providing neuroprotection to a mammal in need thereof by administering an effective amount of xenon (claims 1 and 2). It is the Examiner's position that the instant method of treating a human having aberrant or undesired apoptosis or a disease associated with aberrant apoptosis is inherent in the method of Franks et al. Therefore, instant claims 12, 16 and 18-20 are anticipated.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERNST V. ARNOLD whose telephone number is (571)272-8509. The examiner can normally be reached on M-F 6:15-3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ernst V Arnold/
Examiner, Art Unit 1616